Polio endgame strategy
The challenges for Asia Pacific Region

Vaccinology 2013
1st International Symposium for Asia Pacific Experts
Bangkok, Thailand
November 11-14th, 2013

May Book-Montellano, MD
The fight against Polio has lasted for over 70 years

1938
Creation of the March of Dimes by Franklin Roosevelt to fight against Polio

1955
Francis Field Trial of Salk’s Inactivated Polio Vaccine: the largest clinical trial ever

1988
The World Health Assembly launched the Global Polio Eradication Initiative (GPEI)

1988
Polio Eradication and End Game Strategic Plan 2013-2018 launched by the Global Polio Eradication Initiative (GPEI)

- Launched at 41st World Health Assembly with delegates from 166 countries
- Initial goal: “Eradicate wild-type poliomyelitis globally by the year 2000”
- Spearheaded by WHO, CDC, UNICEF and Rotary International

Vaccine switch urged for polio endgame
Inactivated virus vaccine could deliver the final blow.
Polio cases in the world in 2013

http://www.polioeradication.org/Dataandmonitoring.aspx
### Wild Poliovirus (WPV) cases

#### Polio this week - As of 30 October 2013
Cluster of 22 acute flaccid paralysis (AFP) cases on 17 October 2013 in the Syrian Arab Republic, wild poliovirus type 1 (WPV1) has been isolated from 10 of the cases under investigation.

- South Sudan has been removed from the list of countries with WPV1.

<table>
<thead>
<tr>
<th>Total cases</th>
<th>Year-to-date 2013</th>
<th>Year-to-date 2012</th>
<th>Total in 2012</th>
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<tr>
<td>Globally</td>
<td>322</td>
<td>177</td>
<td>223</td>
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<tr>
<td>- in endemic countries</td>
<td>110</td>
<td>172</td>
<td>217</td>
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<tr>
<td>- in non-endemic countries</td>
<td>212</td>
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<tr>
<td>Country</td>
<td>cVDPV type 1</td>
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<td>cVDPV type 3</td>
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<td>China</td>
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<td>DOR/Haiti</td>
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<td>Total type 1</td>
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<td>Madagascar</td>
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<td>Total type 2</td>
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<td>Yemen</td>
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<td>Cambodia</td>
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<td>Total type 3</td>
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**Polio Eradication in the South-East Asian Region**

*BAN – 2006 and NEP – 2010: WPV outbreaks from India importations*

**MMR – 2007 Type1 Poliovirus outbreak in province Rakhine (district Maungdaw) bordering Bangladesh.**

**Countries without cases >12 months**
- IND-13 Jan 2011 P1
- NEP-30 Aug 2010 P1

**Polio free >5 years**
- BHU-1986 MMR-2007
- BAN-2006 SRL-1993
- KRD-1996 THA-1997
- INO-2006 TLS-1996
- MAL-1994

*Disclaimer: The boundaries and names shown and the designations used on all the maps do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.*
Last indigenous Wild Polio Virus in WPRO

**LEGEND:**
- WPV1 (1997)
- WPV2 (1989)
- WPV3 (1993) *

* WPV3 in 1993 in 3 countries (China, Lao,Viet-Nam) dates of onset to be checked

WPR update: Progress and perspective in Polio Cross Border Meeting on Polio, July 2013 BKK, Thailand

http://www.google.com/url?sa=t&rct=j&q=&esrc=s&frm=1&source=web&cd=2&ved=0CC8QFjAB&url=ftp%3A%2F%2Fftp.wpro.who.int%2Fscratch%2FEPI%2FSEARO%2FCross%2520Border%2520Meeting_BKK%2520Jul%25202013%2520FDAY%252021%2520Regional%2520update%2520on%2520progress%2520and%2520perspective%2520Polio%2520(Boualaml).pptx&ei=Ekp8UobOJ6rAiQe3hoDADQ&usg=AFQjCNRcSYRq5-QBIdcLV3FKplVXyPVIQg&bvm=bv.56146854,d.aGc
Imported Wild Polio Virus in WPRO

LEGEND:
- WPV1 (2011)
- WPV2
- WPV3 (1986)

WPR update: Progress and perspective in Polio Cross Border Meeting on Polio, July 2013 BKK, Thailand
VDPV (vaccine-derived polio virus) in WPRO

**LEGEND:**
- cVDPV1 (2001)
- cVDPV3 (2006)
- cVDPV2 (2011-2012)

WPR update: Progress and perspective in Polio Cross Border Meeting on Polio, July 2013 BKK, Thailand
Cross border meeting highlights risks to polio eradication (Bangkok, Thailand)

http://www.searo.who.int/entity/immunization/topics/polio/crossboarder_meeting_polio_sear_wpr/en/index.html#
Cross border meeting: Challenges in SEA Region

• SEA Region is rapidly approaching polio-free certification in February 2014.

• Efforts towards maintaining its polio-free status remain a high priority in the region.

• Challenges identified:
  – Circulating wild poliovirus
  – Vaccine derived polioviruses (VDPVs) represent an additional threat to the polio eradication initiative.

http://www.searo.who.int/entity/immunization/topics/polio/crossborderer_meeting_polio_sear_wpr/en/index.html#
While three countries are still endemic for WPV circulation, more are still afflicted by PV circulation:

- WPV type 2 circulation has been eradicated since 1999
- WPV types 1 & 3 circulation seems to be under extinction
- Ongoing cVDPV outbreaks indicate that
- VDPV Type 2 are actively circulating, therefore can we really say that PV type 2 is eradicated
- Poliomyelitis due to type 2 is not eradicated
- The total number of AFP cases due to WPV will probably be lower in 2013 than those due to VDPVs and VAPP

Source: [www.polioeradication.org](http://www.polioeradication.org)
Intrinsic characteristics of OPV are challenging the eradication of polioviruses circulation and eradication of poliomyelitis disease

- **VAPP (Vaccine-associated Paralytic Polio)**
- **Vaccine-Derived Polioviruses (VDPV)**

  - The by-dose SC in vaccinees is not consistent and low in many settings and the by-dose (and cumulated) vaccine effectiveness is sub-optimal despite vaccination programs relying on > 10 consecutive OPV administrations up to 5 years of age
    - The use of mOPV$_1$, mOPV$_3$ and bOPV$_{1&3}$ products do improve the immune responses induced by OPV against polioviruses types 1 and 3, and therefore do improve their effectiveness
VAPP: a rare but serious and inevitable Adverse Event associated with OPV

- AFP case with neurologic deficit at 60 days after onset of symptoms caused by a vaccine-related poliovirus
- Due to diffusion from the gut of a mutated vaccine virus having re-acquired the neurovirulence phenotype
- Clinically indistinguishable from poliomyelitis induced by WPVs
- Recognized as early as 1962 in the US
- May affect both OPV vaccinees & contacts of OPV recipients
  - Most of the time, primo-vaccinees
- Estimation of risk to develop VAPP depends on:
  - First-dose versus subsequent-dose recipient (progressive immunity decreases the risk), OPV-vaccinated contact
  - When/How OPV is administered: birth vs later; routine vs NIDs/SIAs
  - Level of exposure to WPVs
- Best estimate of VAPP incidence following tOPV is 2 (US) to 4 (India) VAPP cases per million birth cohort per year
  - 250 to 500 VAPP cases per year (estimation)
  - Type 3 (50%) > Type 2 (40%) > Type 1 (10%)
Vaccine-Derived Polioviruses (VDPV): An inevitable consequence of the use of OPV with suboptimal vaccination coverage

- VDPV are polioviruses presenting more than 1% (0.6% for type 2) genomic divergence from the parental Sabin poliovirus VP1 sequence
  - Accumulation of mutations of the replicating Sabin virus within the vaccinee’s guts or vaccinee’s contact’s guts for > 1 year
  - Reverted to neurovirulence (or paralyticogenicity) and transmissibility

- iVDPV is a VDPV isolated from an immune deficient individual who has become a long-term excretor (several decades)
  - More and more cases are detected in the context of an AFP onset

- cVDPV (circulating VDPV) is a VDPV with adequate conditions for sustained transmission in a human community and responsible for at least >2 AFP cases
  - Factors favoring emergence and spread of cVDPVs
    - Low vaccination coverage with OPV; Poor sanitation conditions; High population density; Lack of competition from WPV circulation; Tropical conditions
WHO/GPEI strategy based on the use of bOPV1&3 and IPV for a phased eradication of circulation of poliovirus

An “OPV-followed-by-IPV” sequential regimen

Switch from tOPV to bOPV$_{1&3}$ for routine immunization

- To address the cVDPV$_2$ risks
- To maximize vaccine effectiveness against type 1 and 3 (better immunogenicity with bOPV$_{1&3}$)

Introduction of IPV six months ahead of the tOPV-to-bOPV$_{1&3}$ switch

- To boost immunity (particularly intestinal mucosal immunity through sIgA response and passively transuded IgG) against types 1 & 3 in previously OPV-primed subjects
- To prime against type 2 when tOPV will be no longer used
- At least one dose of IPV
- IM and ID routes under consideration
Scientific rationale behind the WHO/GPEI strategy

- Ability of IPV to act as a booster and to induce high levels of circulating poliovirus neutralizing antibody
  - Transudation of circulating IgG onto the surface of intestinal mucosa

- Ability of the IPV boost to induce a gut homing effect of specific memory B cells at mucosal surfaces
  - Secretion of sIgA from intestinal mucosa

- Immunological priming effect of one dose of IPV in naïve individuals

- Capacity of vaccinees to neutralize PV at mucosal surface
  - Protection against AFP
  - Excrete less and for shorter periods PV if infected therefore limiting the circulation of PV within communities
Countries’ Challenges Identified

- Persistent pocket of immunity/ surveillance gaps
- Sub-optimal completeness & timeliness in the AFP data reporting
- IPV products not yet registered in some GAVI or non-GAVI countries
- Tight timeline: Countries need to express in coming months, their vaccine switch modalities (national plan of action)
- Potential financial constraints related to the IPV vaccine introduction
Different schedules and different polio vaccines used
LEGEND:

- **GAVI**: GAVI eligible or graduating countries
- **Non-GAVI**: Non-GAVI

<table>
<thead>
<tr>
<th>GAVI</th>
<th>Non-GAVI</th>
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<tbody>
<tr>
<td>Cambodia</td>
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<td>Vanuatu</td>
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*GAVI eligible or graduating countries*
Other Challenges

- Timeline: tight!
- Other competing vaccine targets/introduction in 2014
- Registration of IPV and bOPV in the countries
- Supply (IPV, bOPV)
- Funding and Programmatic implementation
- Maintain/increase vaccination coverage
- Education and training
- Security/Political support
WHO Polio Free Certification Timeline for SEA:

• Dates for the next meetings of the SEA-RCCPE:
  – 28-30 October 2013 (Kathmandu, Nepal)
  – 24-27 February 2014 (New Delhi, India)

• Provide in-country support to the NCCPE:
  – Nepal: 21-23 January 2013 (completed)
  – Timor-Lestes: 11-15 February 2013 (completed)
  – Bhutan: 8-10 April 2013
  – Indonesia: 1-3 May 2013
  – Sri Lanka: 10-12 June 2013
Polio end-game Wes-Pac key dates

Planned events

23-25 July: interregional border workshop for Mekong countries.
15-17 September: PIC Sub Regional certification Committee Meeting
11-14 November: 19th Regional Certification Commission meeting, Manila

Next steps

By end Q3 2013: Draft national end-game plans of action developed
By end Q1 2014: National plan of action
By Q2 2014: WPRO Regional strategic operational plan to be compiled

Viet-Nam; China; PGN; Laos; have already requested technical support
“To operationalize the endgame strategic plan at the national level, a multisectoral sequenced and coordinated effort will be required to get political and other key stakeholders’ endorsement and commitment.

Therefore coordinated partnership support will be critical to successfully implement endgame strategies on the very tight timeline required (introduction of IPV by October 2015; replace tOPV with bOPV by April 2016). Some countries may wish to convene a task force to coordinate this effort.”
TAG recommendations: country specific

- Countries to draft **national polio endgame strategic plan of action**.
- GPEESP 2013-2018 should serve as a blueprint for developing country-specific plans, with emphasis on introduction of **at least one dose of IPV by October 2015** and replacing tOPV with bOPV by April 2016.
  - **By November 2013**, each country should provide to the RCC a **provisional schedule for IPV and dates for introduction of IPV and bOPV to facilitate regional vaccine forecasting**, and a **provisional estimate of resource requirements**.
  - The plan should include the financial resource requirements
  - The plan should include a timeline and reporting system to monitor the progress of country plan implementation.

- The TAG recommends that countries planning introduction of IPV make provisions to secure long-term financing for the vaccine.
- The TAG encourages countries to initiate, as soon as possible, dialogue to develop national consensus with NITAGs and other relevant technical committees and multisectoral departments
Member States will need to focus their efforts on priority areas while progress towards regional certification continues:

- Maintain **high population immunity** through routine immunization and campaigns where appropriate
- Ensure **surveillance networks** remain highly sensitive to detect any poliovirus
- Conduct **risk assessment reviews** for importation and circulation of wild poliovirus
- Completing required **documentation for laboratory containment** of all poliovirus
- Plan for **end game strategy** and eventual **switch of vaccine** and introducing inactivated polio vaccine

Conclusions

- AFP cases due to WPV and VDPV are still occurring in Asia and Africa

- Several factors are hindering poliomyelitis eradication
  - Poor effectiveness of OPV in some settings
  - VAPP and cVDPV

- World Health Organization (WHO) recognizes that the Polio Eradication objectives are achievable through the parallel pursuit of wild poliovirus eradication, VAPP and cVDPV elimination while planning for the backbone of the polio effort to be used for delivering other health services to the world’s most vulnerable children
  - Important value of IPV during both pre- and post-eradication
  - Gradual switch to IPV will help make the transition smooth and effective